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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/511,282	04/08/2005	Katariina Maria Hutterer	PB0217	1837

7590 07/06/2009

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Patent Department
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EXAMINER	
DIETERLE, JENNIFER M	
ART UNIT	PAPER NUMBER
1795	

MAIL DATE	DELIVERY MODE
07/06/2009	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/511,282	HUTTERER ET AL.	
	Examiner	Art Unit	
	Jennifer Dieterle	4111	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *11 May 2009*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *14-18 and 20-22* is/are pending in the application.

4a) Of the above claim(s) *1-13 and 19* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *14-18 and 20-22* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☒ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Response to Amendment

Applicant's amendment of 5/11/2009 does not render the application allowable.

Comments

1. The objection to the claims has been overcome by Applicant's amendment thereof.

Status of Claims

Claims 1-13 have been withdrawn.

Claims 19 has been canceled.

Claim 14, 20 and 21 have been amended.

Claims 14-18 and 20-21 are being addressed.

Status of the Rejections

2. All rejections from the previous office action are withdrawn in view of Applicant's amendment. New grounds of rejections under 35 U.S.C. 103(a) are necessitated by amendments. Unlu et al. ("Difference gel electrophoresis: A single gel method for detecting changes in protein extracts," Electrophoresis 1997, vol. 18, pages 2071-2077) is being cited and relied on for the first time in this office action. Its use was necessitated by the amendment to the claims.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

The factual inquiries set forth in *Graham* v. *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

3. Claims 14-18 and 22 are rejected under 35 U.S.C. 103(a) as being obvious over Issaq et al. (“Multidimensional high performance liquid chromatography-capillary

electrophoresis separation of a protein digest: An update", 2001) in view of Unlu et al. ("Difference gel electrophoresis: A single gel method for detecting changes in protein extracts," Electrophoresis 1997, vol. 18, pages 2071-2077) as evidenced by Rybicki et al. ("SDS Polyacrylamide Gel Electrophoresis (SDS-PAGE)", University of Cape Town, 2/29/04).

Regarding claims 14 and 18, Issaq et al. teach a separation and detection technique utilizing high performance liquid chromatography (hereinafter "HPLC") and parallel gel capillary electrophoresis (abstract). Issaq et al. teach the process of first injecting the digest (sample) into the HPLC instrument and collecting the fractions. The collected fractions were analyzed by UV-absorption and the samples were derivatized with fluorescein isothiocyanate prior to capillary electrophoresis (hereinafter "CE") (page 1133).

Issaq et al. teach the separation of an enzymatic digest mixture of two proteins, but does not teach the separation of a protein which is the larger part of the digest. Issaq et al. also does not teach that the second dimension of separation is performed using a size-based sieving matrix.

Unlu et al. teach the use of cell lysate for protein separation using 2D polyacrylamide gel electrophoresis (abstract; page 2072, col. 2, section 2.4). Applicants' define cell lysate in their specification in "Example 2" as a sample that has been homogenized. Unlu et al. teach a sample of Ecoli (Ecoli contains proteins) which is homogenized using DTT, urea, and CHAPS like that of Applicants. Additionally, Applicants' specification figure 5 shows the use of an Ecoli extract.

Additionally, Unlu et al. teach the use of 2-D separation to separate and detect proteins in a complex protein mixture by first using isoelectric focusing (IEF), which separates proteins according to their pH gradients, and then by SDS/Tris polyacrylamide gel electrophoresis (SDS/PAGE) which separates according to size (page 2071, col. 1,Section I).

It is well known in the art that polyacrylamide gel provides a means of separating molecules based on size as a gel is porous and acts as a sieve by retarding or obstructing the movement of large macromolecules (i.e. proteins) and allows smaller molecules to migrate freely (see Rybicki et al.)

Therefore, it would have been obvious to one skilled in the art to modify the method of Issaq et al. to detect proteins from a cell lysate sample as taught by Unlu et al. because a cell lysate contains proteins and when the sample is lysated/homogenized the contents within the cell/sample are released (i.e. proteins) and are able to be detected. It would also have been obvious to one skilled in the art to modify the method of Issaq et al. to use capillary gel electrophoresis as the second method of separation as taught by Unlu et al. because 2D polyacrylamide gel electrophoresis has become the primary tool for analysis of complex protein mixtures due to its high resolution and sensitivity (page 2071, col. 1,Section I).

Regarding claims 15 and 16, Issaq et al. teach that an allura red dye is added to each of the wells prior to CE in order to create a fluorescence spectra (page 1134, bottom of the first column). While the first phase of separation involving HPLC in Issaq et al. use UV absorption to analyze the sample, it could employ a dye and detect the

separation based on fluorescence as it does with the CE step. Substituting a dye detection method for UV absorption will not yield different results. The sample will still undergo separation and the separation can be detected. Although Issaq et al. do not disclose using a dye to detect separation based on HPLC, the mere duplication of parts has no patentable significance unless a new and unexpected result is produced. *See In re Harza*, 274 F.2d 669, 124 USPQ 378 (CCPA 1960), See also MPEP 2144.04(VI)(B).

Additionally, it is well known in the art to use dye labeling with electrophoretic methods as evidenced by Unlu et al. teach the use of dyes (page 2071, col. 2). Two protein samples are prelabeled with two cyanine dyes, thus enabling one to run two different samples on the same gel in both dimensions. Hence, the two samples are subjected to the same procedure and environment throughout the experiment. Protein spots can be detected by fluorescence imaging immediately after electrophoresis with a sensitivity equal to silver staining.

Regarding claim 17, see discussion regarding claims 15 and 16 above. Additionally, the use of a control, known or standard molecule to use a baseline for comparison or calibration standard is well known in the separation art. In Applicants' Example 1 they reference using Sigma catalog number F3401 fluorescently labeled protein standard which is well known in the art.

Therefore, it would have been obvious to one skilled in the art to run a baseline dye labeled control labeled sample to determine a reference point from which measurement/comparisons of proteins can be made.

Regarding claim 22, Issaq et al. teach the use of a 96 well microtiter plate in which the capillaries are set-up side by side (page 1133, column 2).

4. Claim 20 is rejected under 35 U.S.C. 103(a) as being unpatentable over Issaq et al. and Unlu et al. in view of Dolnik et al. (Galactomannans as a sieving matrix in capillary electrophoresis, Electrophoresis, 2001, vol. 22, pages 707-771).

Regarding claim 20, Issaq et al. teach a two phase separation of a biological sample using CE as the second method of separation, however, Issaq et al. do not teach the use of galactomannan as a sieving matrix in the CE separation.

Dolnik et al. teach the use of galactomannans as a sieving matrix in capillary electrophoresis (abstract).

Therefore, it would have been obvious to one skilled in the art to modify the method of Issaq et al. to use galactomannans as the sieving matrix as taught by Dolnik et al. because galactomannans are known in the art and have been used as sieving matrices for the separation of proteins (page 708, col. 1, second paragraph).

5. Claim 21 is rejected under 35 U.S.C. 103(a) as being unpatentable over Issaq et al. and Unlu et al. in view of Zhu et al. (US 5,545,302).

Regarding claim 21, Issaq et al. teach a two phase separation of a biological sample using CE as the second method of separation, however, Issaq et al. do not teach the use of dextran as a sieving matrix in the CGE separation.

Zhu et al. teach the use of dextran as a sieving matrix in capillary gel electrophoresis (abstract). Applicant's example 1 and 4 show that polyacrylamide gel lines the capillary and then a sieving mixture of dextran fills the remainder. Zhu et al.

teach the same method of electrophoresis utilizing a polyacrylamide gel lines the capillary and then a sieving mixture of dextran (col. 8, lines 63-68; col. 9, lines 1-13).

Therefore, it would have been obvious to one skilled in the art to modify the method of Issaq et al. to use dextran as the sieving matrix as taught by Zhu et al. because dextran suppresses electroendosmosis (abstract).

Response to Arguments

Applicant's arguments with respect to claims 14-18 and 20-22 have been considered but are moot in view of the new ground(s) of rejection.

6. Applicant's arguments filed 5/11/2009 have been fully considered but they are not persuasive. Applicant's response that Issaq et al. fails to teach the separation of proteins the biological sample being a blood sample is acknowledged. In light of Applicant's amendments to the claims, new references, such as Unlu et al., were introduced and teach the use of "cell lysate," "gel matrix" and "proteins" as shown in the amended claims. Applicant's response is no longer persuasive in light of the new art.

7. Applicants' argue that the dye used in Issaq et al. is unrelated to the claimed invention; however, no explanation has been given as to why the dye disclosed in Issaq et al. is different from applicants' invention. Applicants' in claim 15-16 claim the general concept of "dye labeling" which is well known in the separation art. Issaq et al. uses a red dye to label the sample which meets the limitation of "dye labeling."

Conclusion

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Jennifer Dieterle whose telephone number is (571) 270-7872. The examiner can normally be reached on Monday thru Friday, 8am to 5pm (EST).

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Brian Sines can be reached on (571) 272-1263. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for

published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

JMD
6/29/09

/Brian J. Sines/

Supervisory Patent Examiner, Art Unit 1795